

Error-Prone Cellular Automata as Metaphors of Immunity as Computation

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Abstract

Modeling the immune system so that its essential functionalities stand out without the need for every molecular or cellular interaction to be taken into account has been challenging for many decades. Two competing approaches have been the clonal selection theory and the idiotypic-network theory, each stemming from a relatively separate set of principles. One recent perspective holding the promise of unification is that of immunity as computation, that is, of immunity as the process of computing the state of the body so that protection can be effected, as well as boosted through learning. Here we investigate the use of cellular automata (CA) as the core abstraction supporting this new perspective. Our choice of CA for this role is based on the potential variety of basins in a CA attractor field. Associating each basin with a consistent set of body states, and moreover providing for the noisy evolution of the CA in time so that jumping between basins is possible, have provided the necessary backdrop. Given a CA rule to be followed by all cells synchronously, our model is based on a probability with which each cell, at each time step, independently updates its own state differently than the rule mandates. Setting up and solving the corresponding Markov chain for its stationary probabilities have revealed that already in the context of elementary CA there exist rules that, while allowing transitions between basins, display remarkable resiliency in terms of basin occupation. For these rules, the long-run probability that the CA is found in a given basin is practically the same as in the deterministic case when the initial CA state is chosen uniformly at random. We argue that, consequently, our single-parameter CA model may be a suitable abstraction of immunity as computation.

Keywords: Immune system, Cellular automata, Immunity as computation.

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1 Introduction

The immune system is one of the body’s major regulatory systems. Comprising important elements at various physical scales, such as organs, cells, and molecules, the immune system provides defenses against pathogenic bacteria and viruses, identifies and seeks to eliminate abnormally behaving cells before they become established tumors, and carries out tissue restoration as well as various other housekeeping activities. The immune response to invading pathogens, as well as the system’s participation in body maintenance, are the product of learning and self-organization: Beginning with the so-called innate immunity, the immune system is capable of recreating itself along its history while avoiding the pitfalls of autoimmunity [20]. In order to remain fit for such potentially daunting task for as long as possible, the immune system relies on the process known as somatic hypermutation [21], which continually provides the required diversity at the immune-cellular level.

While by virtue of the immune system’s nature as a self-organizing entity it seems safe to view the rise of the various immune functions as a process that proceeds from the bottom up, starting with local interactions at the molecular level, immunity is undoubtedly a systemic process. Explanatory theories of the immune system have therefore oscillated between the very local (with the clonal selection theory [5, 11]) and the very wide (with the elusive idiotypic-network theory [16, 3, 19], based on the idea that many immune-system elements interact with one another much as they do with antigens). A curious (though apt) perspective that might reconcile the two extremes is that the immune system continually “computes” the state of the body (of which it is part), resulting in state alterations as the immune system both acts and learns [6].

Models of the immune system, however, have concentrated on expressing the evolution in time of cell concentrations and other quantities, usually by differential equations (cf., e.g., [10]) but also by discrete-time abstractions akin to cellular automata (CA) [22]. In general such models have been shown to provide a qualitatively convincing picture of how several of the important immune functions arise, or of how the idiotypic network is thought to be organized. But the immunity-as-computation paradigm is to our knowledge yet to be explored, though it should be for at least two reasons that we find quite compelling. The first one is that viewing immunity as resulting from the continual computation of states of the body is bound to require new abstractions through which such states can be represented and manipulated, mathematically or computationally. As a consequence, valuable insight can be expected to emerge. The second reason is that, once suitable state representations have been identified, the possibility of uncertain events that renders the entire system both adaptive and vulnerable can be more easily taken into account.

Here we begin to investigate the use of CA as a suitable abstraction to underlie the study of the immune system as a computational entity. Although choosing CA may seem only natural to unconditional CA enthusiasts, given the impressive plethora of domains to which CA have been applied [27], in our vision there are specific reasons backing our choice. One of them is that, by virtue of

the deterministic character of how CA evolve in time, all CA states for a given finite number of cells and a fixed rule are necessarily partitioned into attractor basins. Viewing CA states as body states and the CA rule as summarizing the computation of body states by the immune system immediately yields an interpretation of each basin as the set of states to which the body is confined once it is born into that basin. Depending on the CA rule in question some basins may express a complex succession of body states while others may seem dull by comparison or merely bespeak decay and disorganization.

Another reason for choosing a representation by CA is that they yield easily to the incorporation of uncertainty. This can be achieved in many ways, our choice being to allow each cell, at each time step, to disobey the CA rule in use and change its state differently than the rule mandates. We model this possibility by a single probability parameter, denoted by p . The usual, deterministic CA world is recovered by setting p to 0, but proceeding otherwise (i.e., choosing $p > 0$) immediately opens up new doors. Specifically, every CA state becomes reachable from every other state, whence it follows that the aforementioned attractor basins are no longer unreachable from one another during the CA dynamics but rather allow the body whose states are the CA states to journey through a rich variety of domains (health, disease, recovery, etc.), however unlikely the transition from one to another may be. It also follows that the attractor dynamics inside a basin is no longer inevitable, and likewise that the periodic attractor lying at a basin's core is not inescapable.

The question we seek to answer is the following. Given a CA rule and an attractor basin in the corresponding CA-state space, what is the probability that, in the long run, the CA state is part of that basin? Unlike other studies that model uncertainty in a manner similar to ours (cf., e.g., [23] and references therein), answering this question relies not on analyzing spatiotemporal patterns of CA evolution but rather on solving Markov chains for their stationary distributions. This is computationally strenuous, but for modestly sized systems we show that there do exist CA rules for which the added uncertainty, while allowing the desired transitions between CA states of different basins to occur, nevertheless tends to confine the CA dynamics to within the same basin where it would unfold if no uncertainty had been added but initial conditions were random.

We proceed in the following manner. We present our model, along with its main properties, in Section 2. This is followed by our methodology in Section 3, results in Section 4, and discussion in Sections 5 and 6. We conclude in Section 7.

2 Model

We consider binary CA, i.e., CA whose cell states are either 0 or 1. If n is the number of cells, assumed finite, then the number of distinct CA states is 2^n . All cells update their states at all times synchronously (i.e., in lockstep) based on the same rule, which can be thought of as a table of binary outputs indexed by $(\delta + 1)$ -bit inputs. Here δ is the size of a cell's neighborhood, the same for all

cells, so a cell's new state depends on its own current state and on its neighbors' current states. Each rule's size is $2^{\delta+1}$, so there exist $2^{2^{\delta+1}}$ distinct rules. Fixing the rule to be used gives rise to a function f mapping each CA state in $\{0, 1\}^n$ into another state in the same set.

Our model is based on turning deterministic CA into probabilistic ones. We do this by introducing a probability, p , with which each cell, at each time step, disobeys the rule's prescription for its next state independently of all other cells. So, if x denotes a cell's next state and the CA rule's current prescription for the value of x is $b \in \{0, 1\}$, we have

$$x := \begin{cases} 1 - b, & \text{with probability } p; \\ b, & \text{otherwise.} \end{cases} \quad (1)$$

Now let $i, j \in \{0, 1\}^n$ be any two CA states and let $H_{i,j}$ be the Hamming distance between them (i.e., the number of cells at which i and j differ). Additionally, let $k_i = f(i)$, i.e., k_i is the CA state that follows i in the deterministic dynamics for the rule at hand. Once we introduce the probability p , the probability that CA state i is followed by j , denoted by $p_{i,j}$, is

$$p_{i,j} = p^{H_{j,k_i}} (1 - p)^{n - H_{j,k_i}}. \quad (2)$$

Readily, letting $j = k_i$ yields $H_{j,k_i} = 0$, and consequently $p_{i,j} = (1 - p)^n$. This is the probability with which i is followed by k_i , that is, the probability that at any given time step the deterministic prescription is respected.

Thus, while using $p = 0$ clearly recovers the traditional, deterministic dynamics (since $p_{i,j} = 1$ if $j = k_i$ and $p_{i,j} = 0$ otherwise), using $p > 0$ lets the CA dynamics be described as a discrete-time Markov chain on the CA states and having $P = [p_{i,j}]$ for transition-probability matrix. To see this it suffices to verify that the elements of P sum up to 1 on any row. That is, fixing i yields

$$\sum_{j \in \{0,1\}^n} p_{i,j} = \sum_{h=0}^n \binom{n}{h} p^h (1 - p)^{n-h} = 1 \quad (3)$$

(because k_i is fixed along with i and differs at h cells from $\binom{n}{h}$ of the 2^n CA states for any given number h of cells). Moreover, for $p > 0$ every element of P is nonzero and therefore the chain is ergodic, meaning that, regardless of how likely it is for any given CA state to be the initial state, in the long run the CA is found in state i with the stationary probability π_i given by $\pi = \pi P$, where $\pi = [\pi_i]$ is a row vector.

2.1 On symmetry

By Eq. (1), letting $p = 1$ also implies deterministic behavior, but following the rule that is complementary to the one that is followed when $p = 0$. That is, one rule sets x to b if and only if the other sets it to $1 - b$. A similar type of symmetry occurs between the case in which $p > 0$ and that in which $1 - p$ is used instead.

To see this, first let \bar{l} denote the complement of CA state l (i.e., adding any cell's state in l to its state in \bar{l} yields 1). It clearly follows that $H_{l,j} + H_{\bar{l},j} = n$ for any CA state j . Now recall that Eq. (2) refers to a specific CA rule and to each cell disobeying it with probability p at each time step. Rewriting the equation for the complementary rule and also letting it be disobeyed with probability $1 - p$ instead has no effect on the value of $p_{i,j}$, since

$$(1 - p)^{H_{j,\bar{k}_i}} p^{n - H_{j,\bar{k}_i}} = (1 - p)^{n - H_{j,k_i}} p^{H_{j,k_i}}. \quad (4)$$

Thus, studying the case of any given rule under p leads to the same Markov chain as studying the complementary rule under $1 - p$, and consequently to the same stationary probabilities on the CA states.

Typically our interest lies in small values of p , which makes the case of (the correspondingly large) $1 - p$ even more remarkable, at least at the level of CA states. At the higher level of the attractor basins, however, no equivalence can in general be expected: The probability that the CA is found in a particular basin in the long run depends on how the CA states cluster into basins and in general this happens differently for a given rule and its complement.

Nevertheless, there do exist rule pairs that display equivalent behavior for the same value of p . We identify these pairs by first introducing a transformation between CA states, call it g , and requiring that one of the rules in the pair lead the CA from state i to state k_i if and only if the other rule leads the CA from state $g(i)$ to state $g(k_i)$. Any rule pair satisfying this requirement is such that the corresponding sets of attractor basins, one for each rule, are structurally equivalent to each other. If, moreover, we require $H_{j,k_i} = H_{g(j),g(k_i)}$, then we also have $p_{i,j} = p_{g(i),g(j)}$. What results from this is that, in the long run, the CA is found in any given basin of one of the rules with the same probability that it is found in the equivalent basin of the other rule.

Rule pairs like this are important in our context because they have the potential of reducing the number of rules that have to be analyzed. This is so because, even though the two sets of stationary probabilities on the CA states are in general distinct, when the probabilities are summed up inside any basin of one of the rules the result is the same as that for the other rule's equivalent basin. One transformation g for which every rule has a counterpart with which it satisfies the two requirements above is negation, i.e., adding any cell's state in i to its state in $g(i)$ yields 1. Another one is reflection, i.e., the c th cell's state in i is the same as the $(n - c + 1)$ th cell's state in $g(i)$ for every $c \in \{1, 2, \dots, n\}$.

2.2 A special case

By Eq. (2), letting $p = 0.5$ leads to $p_{i,j} = 1/2^n$ regardless of i, j , or the rule being used. From this it follows that $\pi_i = 1/2^n$ for every i , so the CA is equally likely to be found at any state in the long run. However, our transition-probability matrix P for this particular value of p is not the only one leading to the uniform distribution over the CA states: In fact, this happens if and only if the matrix is doubly stochastic (i.e., its elements add up to 1 column-wise just as they do

row-wise) and implies an ergodic chain. An example is obtained by letting

$$p_{i,j} = \begin{cases} 1/\binom{n}{\tau}, & \text{if } H_{i,j} = \tau; \\ 0, & \text{otherwise} \end{cases} \quad (5)$$

for any number τ of cells [24] (but note that our $p = 0.5$ case is not equivalent to choosing any particular value for τ).

2.3 The general case

Our model is a special case of the so-called probabilistic CA (PCA), in which a cell's next state is no longer given by the customary deterministic rule but instead is chosen probabilistically as a function of the cell's and its neighbors' current states. Our particular type of PCA relies on the probabilistic decision summarized in Eq. (1), itself dependent on a specific deterministic rule (unlike most PCA, in whose case no deterministic rule plays any role).

Placing our model within the wider class of PCA is important because they have been viewed as prototypes of many important systems, both physical and computational, in a way similar to that in which immunity may come to be characterized as a computational process. Examples of such systems include the spin lattices of statistical physics [9, 4, 14, 12, 18] and, more generally, the Markov and Gibbs random fields [1] that, together with various asynchronous state-update schemes [15, 2], underlie many of the so-called probabilistic graphical models (such as Bayesian networks and hidden Markov models) in artificial intelligence [17].

3 Methods

Given a deterministic CA rule and the number n of cells, let m denote the number of attractor basins into which the set $\{0, 1\}^n$ is partitioned. We denote these basins by B_1, B_2, \dots, B_m . For the case in which the rule in question may be disobeyed by any cell at any time step according to Eq. (1) with $p > 0$, our aim is to calculate the probability that, in the long run, the CA is found in some state of a given basin $B \in \{B_1, B_2, \dots, B_m\}$. Denoting this probability by π_B , we clearly have

$$\pi_B = \sum_{k_0 \in \{0,1\}^n} \pi_{B|k_0} \Pr(k_0), \quad (6)$$

where $\pi_{B|k_0}$ is the conditional probability that in the long run the CA is found in some state in B , given that it started at state k_0 , and $\Pr(k_0)$ is the probability that it did start at k_0 . However, it follows from our discussion in Section 2 that $\pi_{B|k_0}$ is actually unaffected by k_0 and can be obtained by adding up π_k , the stationary probability of CA state k in the associated Markov chain, for all $k \in B$. We then have

$$\pi_B = \sum_{k \in B} \pi_k, \quad (7)$$

regardless of how we choose the initial state k_0 , i.e., regardless of $\Pr(k_0)$ for any k_0 .

All our analyses in the forthcoming sections are based on comparing π_B to the corresponding probability when $p = 0$, that is, when evolution is deterministic. We denote this probability by σ_B and the corresponding conditional probability, given k_0 , by $\sigma_{B|k_0}$. Readily,

$$\sigma_{B|k_0} = \begin{cases} 1, & \text{if } k_0 \in B; \\ 0, & \text{otherwise} \end{cases} \quad (8)$$

and

$$\sigma_B = \sum_{k_0 \in \{0,1\}^n} \sigma_{B|k_0} \Pr(k_0) = \sum_{k_0 \in B} \Pr(k_0), \quad (9)$$

so σ_B is clearly dependent upon how k_0 is chosen. We continue by assuming that this happens uniformly at random, that is, $\Pr(k_0) = 1/2^n$ for every k_0 , whence we obtain

$$\sigma_B = \frac{|B|}{2^n}. \quad (10)$$

Thus, σ_B results trivially from the uniform distribution over all CA states (we simply add it up for all states in basin B).

Obtaining π_B for every basin B requires the system $\pi = \pi P$ to be solved, subject to the constraints that $\pi_i > 0$ for all $i \in \{0,1\}^n$ and $\sum_{i \in \{0,1\}^n} \pi_i = 1$, for each desired combination of n , CA rule, and $p > 0$. We have used the solver that is freely available as part of the Tangram-II modeling tool [8]. This solver employs state-of-the-art techniques for the above determination of π given P , but in our case P is a $2^n \times 2^n$ matrix with no zeroes and no facilitating symmetries or structure. Thus the solution process has been very time-consuming, which has constrained n to the modest values of 10 through 12. For the record, we mention that, depending on the CA rule at hand, stepping up to $n = 13$ would demand nearly two months per run on an Intel Xeon E5-1650 at 3.2GHz with enough memory to store the entire 8192×8192 system at all times. This, unfortunately, has proven infeasible.

4 Results

Henceforth we let \mathcal{B} denote the set $\{B_1, B_2, \dots, B_m\}$ of all basins for a given CA rule and a fixed value of n . We compare the distributions $\pi_{B_1}, \pi_{B_2}, \dots, \pi_{B_m}$ and $\sigma_{B_1}, \sigma_{B_2}, \dots, \sigma_{B_m}$ by means of the Hellinger distance between them, denoted by $H(\pi, \sigma)$ and given by

$$H(\pi, \sigma) = \sqrt{1 - \sum_{B \in \mathcal{B}} \sqrt{\pi_B \sigma_B}}. \quad (11)$$

Using the Hellinger distance to compare the two distributions is convenient not only because it truly is a distance function but also because it is always such

that $0 \leq H(\pi, \sigma) \leq 1$. In fact, clearly $H(\pi, \sigma) = 0$ if and only if $\pi_B = \sigma_B$ for all $B \in \mathcal{B}$ and $H(\pi, \sigma) = 1$ if and only if $\pi_B \sigma_B = 0$ for all $B \in \mathcal{B}$. The latter, however, can never be achieved in our context because both π_B and σ_B are strictly positive for all $B \in \mathcal{B}$.

We also compare the mean and standard deviation of basin sizes as they vary from one distribution to the other. To this end, we use the ratios

$$\rho_{\text{mean}} = \frac{\sum_{B \in \mathcal{B}} \pi_B |B|}{\sum_{B \in \mathcal{B}} \sigma_B |B|} \quad (12)$$

and

$$\rho_{\text{s.d.}} = \sqrt{\frac{\sum_{B \in \mathcal{B}} \pi_B |B|^2 - (\sum_{B \in \mathcal{B}} \pi_B |B|)^2}{\sum_{B \in \mathcal{B}} \sigma_B |B|^2 - (\sum_{B \in \mathcal{B}} \sigma_B |B|)^2}}. \quad (13)$$

Clearly, comparing ρ_{mean} to 1 lets us detect increases or decreases in the mean basin size as we move from using the probabilities $\sigma_{B_1}, \sigma_{B_2}, \dots, \sigma_{B_m}$ to using $\pi_{B_1}, \pi_{B_2}, \dots, \pi_{B_m}$, and likewise for $\rho_{\text{s.d.}}$ with respect to the standard deviation of basin sizes.

These data are given in Tables 1 and 2, the former containing Hellinger distances, the latter containing mean and standard-deviation ratios. All data refer to elementary CA [25], which in the present context corresponds to setting a cell's neighborhood size (δ) to 2, and to an arrangement of cells that is one-dimensional with periodic boundaries (i.e., the first and last cells in the arrangement are neighbors). Moreover, our data encompass all combinations of a unique rule, a CA size $n \in \{10, 11, 12\}$, and a probability $p \in \{0.001, 0.01\}$. By unique rule we mean one that is not equivalent to any other selected rule by negation or reflection. Of the 256 possible elementary-CA rules, 88 are unique in this sense but group with the remaining 168 rules into equivalence classes of size at most 4, or into larger clusters of size at most 8 as two equivalence classes of pairwise complementary rules are joined. Each of the equivalence classes might be represented in our tables by any of its members, but we follow Wuensche and Lesser, who in their atlas [29] use one or two rules of each larger cluster, viz. the rule of least number (in the customary Wolfram sense [25]) and its complement if not already in the first rule's equivalence class. Each table also informs a rule's class (1 through 4) according to Wolfram's well-known qualitative scheme [26].

5 Discussion

As we have seen, disobeying a CA rule independently at each cell with probability p makes the CA dynamics stochastic and puts it between two extremes that, in a sense, are equivalent. One extreme is the $p = 0$ case, i.e., the case in which the rule is not disobeyed at all and the customary deterministic dynamics is followed. In this case, the long-run probability that a randomly chosen CA state is in some basin B is σ_B and stems from the uniform distribution on the CA states provided the initial state is itself chosen uniformly at random. The

Table 1: Hellinger distances.

[illegible]

Table 1: Continued.

Rule	Wolfram class	$H(\pi, \sigma)$ for $n = 10$		$H(\pi, \sigma)$ for $n = 11$		$H(\pi, \sigma)$ for $n = 12$	
		$p = 0.001$	$p = 0.01$	$p = 0.001$	$p = 0.01$	$p = 0.001$	$p = 0.01$
19	2	0.665262	0.455025	0.687454	0.466017	0.706507	0.476426
23	2	0.649786	0.504885	0.674805	0.517551	0.699909	0.532909
24	2	0.151170	0.145988	0.162003	0.156480	0.163455	0.157906
25	2	0.178794	0.142287	0.205302	0.166376	0.240752	0.184615
26	2	0.096811	0.087081	0.092313	0.081963	0.082902	0.073380
27	2	0.078410	0.075206	0.078149	0.075674	0.088139	0.084074
28	2	0.507050	0.293820	0.276705	0.187250	0.554002	0.304611
29	2	0.042041	0.041289	0.044401	0.043618	0.046283	0.045463
33	2	0.128619	0.124749	0.102505	0.099605	0.131497	0.128095
35	2	0.112197	0.095522	0.108425	0.093326	0.136032	0.100919
36	2	0.210118	0.202473	0.212746	0.204591	0.218307	0.209832
37	2	0.217930	0.128618	0.130832	0.085161	0.153067	0.127335
38	2	0.053281	0.051025	0.060564	0.058097	0.058462	0.055931
41	2	0.120070	0.097433	0.115620	0.106492	0.150240	0.107285
43	2	0.299150	0.254258	0.340329	0.279313	0.499819	0.357524
46	2	0.176524	0.167568	0.186924	0.177534	0.196353	0.186419
50	2	0.621971	0.428828	0.434170	0.334403	0.667557	0.448039
51	2	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
57	2	0.271948	0.093908	0.095220	0.034859	0.287305	0.079804
58	2	0.230614	0.194367	0.401245	0.276011	0.410814	0.410734
62	2	0.197845	0.138003	0.132255	0.122913	0.215650	0.117917
77	2	0.649786	0.504885	0.447864	0.375344	0.699909	0.532909

Table 1: Continued.

Rule	Wolfram class	$H(\pi, \sigma)$ for $n = 10$		$H(\pi, \sigma)$ for $n = 11$		$H(\pi, \sigma)$ for $n = 12$	
		$p = 0.001$	$p = 0.01$	$p = 0.001$	$p = 0.01$	$p = 0.001$	$p = 0.01$
94	2	0.306439	0.269040	0.277744	0.242535	0.569790	0.280718
178	2	0.649786	0.504885	0.447864	0.375344	0.699909	0.532909
197	2	0.529675	0.345739	0.285589	0.211139	0.581408	0.362983
198	2	0.522388	0.330289	0.282790	0.203589	0.572138	0.344295
201	2	0.220405	0.209932	0.217887	0.207934	0.221112	0.209812
204	2	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
205	2	0.081927	0.080898	0.082447	0.081349	0.083984	0.082815
210	2	0.007328	0.006725	0.000000	0.000000	0.010027	0.008364
212	2	0.299150	0.254258	0.340329	0.279313	0.499819	0.357524
214	2	0.104722	0.100715	0.138109	0.122696	0.112897	0.094736
217	2	0.120698	0.115389	0.130762	0.125581	0.126279	0.121099
218	2	0.266122	0.259242	0.221638	0.214302	0.265582	0.258562
220	2	0.092624	0.090070	0.092633	0.089882	0.094236	0.091322
222	2	0.081912	0.081363	0.081185	0.080555	0.084533	0.084083
226	2	0.170992	0.148976	0.079509	0.075465	0.196928	0.168250
227	2	0.128235	0.089781	0.076123	0.065573	0.109403	0.072279
228	2	0.322168	0.308522	0.308795	0.298360	0.299346	0.290927
229	2	0.101086	0.096509	0.134254	0.119041	0.115874	0.108862
230	2	0.238324	0.230492	0.258104	0.250046	0.277262	0.268729
<i>232</i>	<i>2</i>	<i>0.649786</i>	<i>0.504885</i>	<i>0.674805</i>	<i>0.517551</i>	<i>0.699909</i>	<i>0.532909</i>
233	2	0.370172	0.311163	0.404103	0.341928	0.420107	0.357435
<i>236</i>	<i>2</i>	<i>0.767929</i>	<i>0.677742</i>	<i>0.790184</i>	<i>0.701010</i>	<i>0.810056</i>	<i>0.722260</i>

Table 1: Continued.

Rule	Wolfram class	$H(\pi, \sigma)$ for $n = 10$		$H(\pi, \sigma)$ for $n = 11$		$H(\pi, \sigma)$ for $n = 12$	
		$p = 0.001$	$p = 0.01$	$p = 0.001$	$p = 0.01$	$p = 0.001$	$p = 0.01$
237	2	0.511025	0.446457	0.532280	0.465832	0.551887	0.483901
240	2	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
241	2	0.161638	0.159585	0.169371	0.167225	0.176764	0.174527
242	2	0.219813	0.216880	0.229854	0.226784	0.239672	0.236473
243	2	0.084915	0.083186	0.088408	0.086590	0.091966	0.090065
244	2	0.253371	0.248050	0.265043	0.259493	0.276340	0.270564
246	2	0.123588	0.121820	0.126632	0.124803	0.133269	0.131387
18	3	0.177219	0.171971	0.098671	0.095609	0.216715	0.200709
22	3	0.051738	0.044548	0.090170	0.077895	0.250064	0.134211
30	3	0.034544	0.016889	0.020255	0.007665	0.038162	0.009492
45	3	0.016456	0.010594	0.000000	0.000000	0.056506	0.004097
60	3	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
73	3	0.294481	0.182849	0.120781	0.107784	0.181444	0.151175
90	3	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
105	3	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
126	3	0.114009	0.110473	0.158805	0.146309	0.140149	0.125633
150	3	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
161	3	0.213897	0.142957	0.046676	0.018741	0.145264	0.101305
182	3	0.118028	0.098982	0.037891	0.030647	0.110355	0.095368
225	3	0.034380	0.020135	0.062034	0.018674	0.488660	0.119769
54	4	0.250242	0.160801	0.078368	0.060045	0.285840	0.138826
193	4	0.066972	0.049254	0.057118	0.030831	0.096156	0.052231

Table 2: Mean and standard-deviation ratios (I: $p = 0.001$; II: $p = 0.01$).

[illegible]

Table 2: Continued.

Rule	Wolfram class	$n = 10$				$n = 11$				$n = 12$			
		ρ_{mean}		$\rho_{\text{s.d.}}$		ρ_{mean}		$\rho_{\text{s.d.}}$		ρ_{mean}		$\rho_{\text{s.d.}}$	
		I	II	I	II	I	II	I	II	I	II	I	II
19	2	3.68	2.95	0.48	1.16	4.28	3.27	0.58	1.33	4.97	3.61	0.70	1.51
23	2	3.33	3.01	0.26	0.75	3.89	3.43	0.32	0.88	4.57	3.92	0.38	1.02
24	2	1.01	1.01	1.23	1.21	0.97	0.97	1.03	1.02	0.97	0.98	0.98	0.98
25	2	1.00	0.99	0.99	1.00	0.87	0.89	1.27	1.22	1.21	1.17	0.99	1.01
26	2	0.92	0.92	1.03	1.03	0.94	0.94	0.98	0.98	0.89	0.90	0.94	0.94
27	2	0.95	0.95	0.97	0.97	0.93	0.93	0.94	0.94	0.94	0.94	0.98	0.98
28	2	2.16	1.78	0.35	0.85	1.22	1.18	0.16	0.48	2.72	2.04	0.46	1.03
29	2	1.03	1.03	1.03	1.03	1.04	1.04	1.06	1.06	1.04	1.04	1.05	1.05
33	2	0.77	0.77	0.85	0.86	0.79	0.79	0.84	0.84	0.77	0.77	0.83	0.83
35	2	1.15	1.13	1.01	1.01	1.00	1.00	0.97	0.97	1.10	1.07	1.00	1.00
36	2	0.57	0.59	0.90	0.90	0.54	0.56	0.86	0.87	0.50	0.52	0.82	0.83
37	2	0.86	0.92	1.18	1.10	0.96	0.99	1.14	1.09	1.03	1.03	0.96	0.96
38	2	0.96	0.97	1.02	1.02	0.96	0.96	1.04	1.03	0.95	0.95	1.00	1.00
41	2	1.04	1.03	0.95	0.97	1.16	1.15	1.12	1.12	0.83	0.89	0.97	1.01
43	2	1.06	1.05	0.86	0.87	1.42	1.38	0.68	0.74	2.08	1.87	0.24	0.65
46	2	0.96	0.96	1.09	1.08	0.97	0.97	1.14	1.13	0.92	0.93	1.03	1.03
50	2	3.29	2.74	0.37	0.94	1.58	1.52	0.14	0.43	4.49	3.43	0.52	1.22
51	2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
57	2	1.28	1.12	0.34	0.83	1.03	1.01	0.28	0.78	1.35	1.12	0.41	0.89
58	2	0.97	0.98	1.00	0.99	1.36	1.30	0.18	0.52	1.35	1.31	0.43	0.43
62	2	1.24	1.17	0.61	0.77	1.31	1.30	1.17	1.16	0.85	0.96	1.04	1.01
77	2	3.33	3.01	0.26	0.75	1.58	1.55	0.10	0.32	4.57	3.92	0.38	1.02

Table 2: Continued.

Rule	Wolfram class	$n = 10$				$n = 11$				$n = 12$			
		ρ_{mean}		$\rho_{\text{s.d.}}$		ρ_{mean}		$\rho_{\text{s.d.}}$		ρ_{mean}		$\rho_{\text{s.d.}}$	
		I	II	I	II	I	II	I	II	I	II	I	II
94	2	0.84	0.87	1.13	1.12	0.90	0.92	1.04	1.03	2.04	1.30	0.66	1.08
178	2	3.33	3.01	0.26	0.75	1.58	1.55	0.10	0.32	4.57	3.92	0.38	1.02
197	2	1.91	1.70	0.28	0.75	1.17	1.15	0.13	0.39	2.30	1.92	0.37	0.94
198	2	2.17	1.85	0.30	0.80	1.22	1.19	0.14	0.42	2.75	2.17	0.41	0.98
201	2	0.91	0.91	1.16	1.15	0.90	0.91	1.12	1.11	0.97	0.96	1.22	1.19
204	2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
205	2	0.97	0.97	1.02	1.01	0.97	0.97	1.00	1.00	0.97	0.97	1.01	1.01
210	2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
212	2	1.04	1.04	0.91	0.91	1.56	1.50	0.85	0.89	2.08	1.87	0.24	0.65
214	2	0.96	0.96	1.05	1.05	0.79	0.82	1.09	1.09	0.97	0.97	0.96	0.97
217	2	0.94	0.94	1.37	1.36	0.92	0.92	1.37	1.35	0.90	0.90	1.12	1.11
218	2	0.59	0.60	0.80	0.81	0.55	0.56	0.79	0.80	0.50	0.52	0.73	0.74
220	2	0.93	0.93	1.02	1.02	0.92	0.92	1.01	1.01	0.91	0.92	1.01	1.01
222	2	0.85	0.85	0.91	0.91	0.83	0.84	0.89	0.89	0.82	0.81	0.88	0.88
226	2	1.08	1.07	0.96	0.97	0.99	0.99	1.00	1.00	1.09	1.08	0.98	0.98
227	2	1.07	1.04	1.00	1.00	1.07	1.05	1.04	1.04	1.08	1.05	1.02	1.01
228	2	0.72	0.74	1.05	1.05	0.69	0.70	0.98	0.98	0.66	0.68	0.91	0.91
229	2	0.96	0.96	1.03	1.03	0.89	0.90	1.01	1.01	0.80	0.81	0.86	0.86
230	2	0.70	0.71	0.86	0.87	0.73	0.74	0.90	0.91	0.70	0.71	0.80	0.81
<i>232</i>	<i>2</i>	<i>3.33</i>	<i>3.01</i>	<i>0.26</i>	<i>0.75</i>	<i>3.89</i>	<i>3.43</i>	<i>0.32</i>	<i>0.88</i>	<i>4.57</i>	<i>3.92</i>	<i>0.38</i>	<i>1.02</i>
233	2	1.39	1.37	0.09	0.28	1.48	1.46	0.09	0.28	1.53	1.51	0.09	0.29
<i>236</i>	<i>2</i>	<i>5.40</i>	<i>5.11</i>	<i>0.24</i>	<i>0.72</i>	<i>6.39</i>	<i>6.01</i>	<i>0.27</i>	<i>0.82</i>	<i>7.57</i>	<i>7.08</i>	<i>0.31</i>	<i>0.92</i>

Table 2: Continued.

Rule	Wolfram class	$n = 10$				$n = 11$				$n = 12$			
		ρ_{mean}		$\rho_{\text{s.d.}}$		ρ_{mean}		$\rho_{\text{s.d.}}$		ρ_{mean}		$\rho_{\text{s.d.}}$	
		I	II	I	II	I	II	I	II	I	II	I	II
237	2	1.88	1.84	0.10	0.31	2.00	1.95	0.10	0.32	2.13	2.07	0.11	0.33
240	2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
241	2	0.80	0.80	0.94	0.94	0.77	0.77	0.90	0.90	0.76	0.76	0.88	0.89
242	2	0.78	0.78	0.96	0.96	0.68	0.68	0.81	0.81	0.69	0.69	0.86	0.86
243	2	0.94	0.94	1.04	1.04	0.92	0.92	1.02	1.02	0.92	0.93	1.00	1.00
244	2	0.96	0.96	0.98	0.98	0.96	0.96	0.99	0.99	0.96	0.96	1.00	1.00
246	2	0.88	0.88	1.10	1.10	0.89	0.90	1.17	1.16	0.92	0.92	1.07	1.07
18	3	0.86	0.86	0.94	0.94	0.90	0.90	1.04	1.04	0.81	0.82	0.64	0.65
22	3	0.94	0.95	0.98	1.00	0.97	0.96	0.99	0.98	0.60	0.79	1.01	1.05
30	3	0.98	0.99	1.05	1.04	0.98	0.99	1.02	1.01	0.99	1.00	1.10	1.04
45	3	0.99	0.99	1.01	1.01	1.00	1.00	1.00	1.00	0.98	1.00	1.00	1.00
60	3	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
73	3	1.08	1.02	1.16	1.09	0.93	0.93	0.90	0.90	0.91	0.86	0.98	0.92
90	3	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
105	3	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
126	3	0.91	0.91	1.07	1.07	0.88	0.88	1.02	1.02	0.87	0.88	0.75	0.78
150	3	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
161	3	0.97	0.98	1.16	1.12	1.02	1.00	0.98	1.02	0.93	0.94	1.05	1.05
182	3	1.02	1.02	0.87	0.88	1.02	1.02	0.95	0.96	1.01	1.00	0.87	0.86
225	3	0.99	0.99	1.02	1.02	1.03	0.99	0.88	1.04	0.39	0.92	1.24	1.14
54	4	0.86	0.90	0.84	0.89	1.03	1.04	1.06	1.05	1.41	1.17	0.86	0.98
193	4	1.03	1.02	0.99	1.00	1.07	1.03	0.92	0.97	0.95	0.97	1.05	1.03

other extreme is that of $p = 0.5$, in which case the long-run probability that the CA is found in basin B is π_B , now stemming from CA-state probabilities that are again uniform but now by virtue of the underlying Markov chain's stationary distribution.

Comparing these two distributions as indicated in Section 4 clearly yields $H(\pi, \sigma) = 0$ and, consequently, $\rho_{\text{mean}} = \rho_{\text{s.d.}} = 1$, regardless of the particular CA rule and CA size being considered. Although these values may look like what we seek (stochastic CA dynamics that, while allowing occasional transitions between basins, let the CA state be found in a same basin for long stretches of time), they are only the product of erratic transitions between the CA states. In fact, for $p = 0.5$ all CA states are equally likely candidates for where the CA is to move next, regardless of where it is currently.

It is instructive to contrast this $p = 0.5$ extreme with the case of any p such that $0 < p < 0.5$. We first rewrite the transition probability $p_{i,j}$ of Eq. (2) as

$$p_{i,j} = (1-p)^n \left(\frac{1-p}{p} \right)^{-H_{j,k_i}}, \quad (14)$$

which for $0 < p < 0.5$ leaves it clear that $p_{i,j}$ decays exponentially with the Hamming distance between j and k_i from the maximum value of $(1-p)^n$. This maximum, as we have noted, is achieved for $j = k_i$, so evolving toward i 's deterministic successor in a single time step is always exponentially more likely than doing it toward any other CA state. Intuitively one might then expect the occurrence of $H(\pi, \sigma) \approx 0$ to be commonplace, but we have found this to be far from the truth. In fact, it all depends on the great richness of detail we can always expect from CA behavior, particularly on how the basins are laid out on the attractor field and whether the CA switches basins in the event that some $j \neq k_i$ is picked when the current CA state is i .

We proceed by singling out some rules for a more detailed discussion. Most of these are highlighted in Tables 1 and 2 with a bold typeface. We occasionally mention specific characteristics of a rule or its basins, and for these the reader is referred to one of the available atlases [29, 28].

First note that, though not commonplace, rules for which $H(\pi, \sigma)$ is indistinguishable from 0 within the six decimal places used in Table 1 do exist. These are class-1 rules 0 and 253; class-2 rules 15, 51, 204, and 240; and class-3 rules 60, 90 (the XOR rule), 105, and 150. For two of these rules, namely 0 and 253, the value of $H(\pi, \sigma)$ is precisely 0, since each of them gives rise to exactly one basin of attraction, call it B_1 , whence it follows that $\pi_{B_1} = \sigma_{B_1} = 1$ no matter what the stationary CA-state probabilities that make up π_{B_1} turn out to be. The value of $H(\pi, \sigma)$ is precisely 0 also for four other rules, namely 15, 51, 204, and 240, but for an entirely different reason. What happens in these cases is that the transition-probability matrix is doubly stochastic, which as we have noted implies that the stationary distribution over the CA states is uniform. For rules 51 and 204, in particular, double stochasticity is a consequence of the matrices' being symmetric (i.e., $p_{i,j} = p_{j,i}$ for all CA states i and j). As for

rules 60, 90, 105, and 150, $H(\pi, \sigma)$ is probably only approximately equal to 0, since the matrices do not seem to be doubly stochastic.

Making the requirement on $H(\pi, \sigma)$ less stringent, for example by replacing indistinguishability from 0 with $H(\pi, \sigma) < 0.1$, turns up further rules: class-1 rules 249, 251, 252, and 254; class-2 rules 12, 26, 27, 29, 38, 205, 210, 220, 222, and 243; class-3 rules 30 and 45; and even one of the elusive class-4 rules, namely rule 193 (more widely recognized through its equivalent by both negation and reflection, the celebrated rule 110, known to be capable of universal computation). The class-1 additions to the list are not really surprising, since in all four cases nearly all CA states cluster into one single basin and therefore our argument above for rules 0 and 253 essentially continues to hold (though approximately). As for the remaining additions (the class-2 through class-4 rules), no readily discernible characteristic seems to stand out that might help explain the relative proximity of the two distributions, not even inside each class.

Aside from these 27 zero or near-zero cases of the Hellinger distance, the remaining 61 rules in Tables 1 and 2, at least for our small sample of n and p values, all give rise to stationary basin probabilities that differ from those of the deterministic case (with initial CA states chosen uniformly at random) to some substantial extent. Singling out some rules on the higher extreme of distance values is not as clear-cut a task as picking the zeroes. As we mentioned earlier, the theoretical maximum distance of 1 can never be achieved for distributions that are strictly positive everywhere, so figuring out the actual maximum for elementary CA is far from a trivial task.

What we do is then to highlight those rules that, across our small sample of n and p values, are on the far side of the (admittedly arbitrary) threshold of $H(\pi, \sigma) = 0.45$. Doing this yields four rules, all in class 2 and italicized in the tables: rules 19, 23, 232, and 236. Once again it is hard to discern any explaining characteristics, but from Table 2 it is clear that all four rules have in common the facts that ρ_{mean} is substantially larger than 1 (but less so as p is increased) and that $\rho_{\text{s.d.}}$ is often smaller than 1 (but growing as p is increased). That is, for small p the distribution is more concentrated on larger basins, all relative to the basin-size distribution arising from the uniform distribution on CA states. This becomes less so as p is increased and the already discussed limit, as p is driven toward 0.5, is approached.

6 Immunity as computation

The present study has hinged on Eq. (1), a simple probabilistic expression of a cell's ability to alter its state differently than the CA rule in use directs it to, at every time step and independently of all other cells. If we view the CA states as states of the body, including the portion of it known as the immune system, then the evolution of CA states in time stands not only for the natural succession of body states but also for the computation of such states by the immune system. Given this context, the adoption of the spatially and temporally local probabilistic alterations to the CA rule given in Eq. (1) is an attempt to summarize

several phenomena originating from the uncertainty that is inherent to every biological process. Such uncertainty drives adaptation, gives rise to diversity as well as disease, and fuels the appearance of idiotypes never before seen in the body and with them the possibility of better immunity through learning.

Though inherently stochastic, our model is also inherently dependent on a fixed CA rule. This is clear already in Eq. (1) itself, where we recall that b stands precisely for the cell's next state according to such a fixed rule. Moreover, although Eq. (1) makes every state update of every cell nondeterministic, globally it is always exponentially more likely to evolve to the CA state the rule mandates than to any other CA state. This means that the clustering of CA states into basins, though no longer unbreachable, is still meaningful and can be exploited as we adopt the modified CA as metaphors of immunity as computation. For example, each basin can be viewed as encompassing CA states that are equivalent from the perspective of the immune system as it computes the state of the body. Some possibilities that come to mind are basins representing a healthy or unhealthy body, others representing a body under recovery through the action of the immune system, and still many others as details are brought into the picture.

In such a setting, changes in the CA state other than those mandated by the underlying CA rule can be interpreted in a variety of ways: e.g., inter-basin transitions may stand for the appearance of or the recovery from diseases, as well as to adaptation into a distinct, though still healthy, set of states; intra-basin transitions, in turn, may represent change that nevertheless does not fundamentally alter the state of the body as far as being healthy is concerned. So far we have explored this landscape by simply asking what the effects of Eq. (1) might be in terms of fundamentally deviating the CA from its traditional excursion into the field of attractor basins under the CA rule in question. We have discovered CA rules in all four of Wolfram's classes for which no fundamental deviation exists while still allowing the CA to occasionally drift in and out of the field's basins.

It is telling that we should find such behavior already in the simplest of CA, viz. elementary CA, and already for the very small ones we investigate in this work. Moving forward will require the investigation of more complex CA, at the same time higher-dimensional, larger, and governed by larger-neighborhood rules. We expect that these enriched scenarios will provide many useful possibilities to characterize immunity as computation. In our view, the importance of characterizations such as this can hardly be overstated: Even as we write, immunotherapy is being hailed as a fundamental breakthrough in cancer treatment (cf. [7], as well as [13] and related content), and theoretical modeling is bound to be instrumental in better understanding this and other applications.

7 Concluding remarks

An important characteristic of our model is its reliance on one single parameter, the probability p . Assuming that it acts at each cell independently of all others has allowed the transition probability $p_{i,j}$, from CA state i to CA state j in a

single step, to be written as in Eq. (2), which in turn implies the ergodicity of the corresponding Markov chain whenever $p > 0$. The model is then conceptually simple, but studying it requires the Markov chain's stationary probabilities to be found, which by virtue of the model's inherent combinatorial growth in the general case quickly becomes computationally burdensome if not downright intractable.

Further research should then first concentrate on looking for those CA rules, if any exist, for which the transition matrix can somehow be simplified so that some facilitating structure emerges. We already know that, for $p < 0.5$, the dominant probability on any of the matrix's rows, say the i th, is $p_{i,k_i} = (1 - p)^n$. Not only this, but $p_{i,j}$ for any $j \neq k_i$ is smaller than p_{i,k_i} by the exponentially decaying factor of $[(1 - p)/p]^{-H_{j,k_i}}$. The key to solving the Markov chain associated with certain rules may lie precisely in ignoring such vanishingly small probabilities, but to our knowledge substantial further research is needed to ascertain this.

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